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From the INTERNATIONAL BUREAU**PCT****NOTIFICATION OF TRANSMITTAL
OF COPIES OF TRANSLATION
OF THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**
(PCT Rule 72.2)

To:

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PATENTANWÄLTE

Date of mailing (day/month/year)

18 November 2004 (18.11.2004)

Applicant's or agent's file reference

96099 a/se

IMPORTANT NOTIFICATION

International application No.

PCT/EP2003/003097

International filing date (day/month/year)

25 March 2003 (25.03.2003)

Applicant

LICHTWER PHARMA AG et al

1. Transmittal of the translation to the applicant.

The International Bureau transmits herewith a copy of the English translation made by the International Bureau of the international preliminary examination report established by the International Preliminary Examining Authority.

2. Transmittal of the copy of the translation to the elected Offices.

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following elected Offices requiring such translation:

AZ, CA, CH, CN, CO, GH, KG, KP, KR, MK, MZ, RU, TM

The following elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, BA, BB, BG, BR, BY, BZ, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EP, ES, FI, GB, GD, GE, GM, HR, HU, ID, IL, IN, IS, JP, KE, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MN, MW, MX, NI, NO, NZ, OA, OM, PH, PL, PT, RO, SC, SD, SE, SG, SK, SL, TJ, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

3. Reminder regarding translation into (one of) the official language(s) of the elected Office(s).

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report.

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO
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Authorized officer

Yolaine Cussac

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Translation

PATENT COOPERATION TREATY

PCT/EP2003/003097



PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 96099 a/se	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP2003/003097	International filing date (day/month/year) 25 March 2003 (25.03.2003)	Priority date (day/month/year) 26 March 2002 (26.03.2002)
International Patent Classification (IPC) or national classification and IPC A61K 35/78, A61P 25/18		
Applicant LICHTWER PHARMA AG		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
- ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 20 October 2003 (20.10.2003)	Date of completion of this report 28 June 2004 (28.06.2004)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP2003/003097

I. Basis of the report

1. With regard to the elements of the international application:*

- ☐ the international application as originally filed
- ☒ the description:
pages _____ 1-17 _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____
- ☒ the claims:
pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____ 1-13 _____, filed with the letter of _____ 13 May 2004 (13.05.2004)
- ☐ the drawings:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____
- ☐ the sequence listing part of the description:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP 03/03097

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-13	YES
	Claims		NO
Inventive step (IS)	Claims	1-13	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-13	YES
	Claims		NO

2. Citations and explanations

1a. The present application relates to the use of *Hypericum perforatum* (St John's wort) and/or *Ginkgo biloba* (ginkgo) and/or *Crocus sativus* (safron) and/or *Panax ginseng* (ginseng) for the treatment of schizophrenia (see main claim 1).

1b. Despite existing transitional forms and mixed conditions in the symptomology of schizophrenia and depression, schizophrenia as a **classic psychotic disorder** should be distinguished from depression as a **classic neurotic disorder**. A scientifically acknowledged basis for this distinction is to be found in ICD-10 (The International Statistical Classification of Diseases and Related Health Problems), in which schizophrenia is distinguished from other classified conditions such as dementia and depression. Consequently, a distinction must be drawn between substances indicated in schizophrenia and substances indicated in depression.

2. In this light, the prior art cited in the written report, relating to the treatment and prophylaxis of depressive disorders or dementia, requires revision.

/...

D1 (EP-A-1 034 782) relates to the treatment of depression, which is distinguished from schizophrenia along the lines set out in point 1b. above, being a psychiatric condition the genesis of which is different from that of schizophrenia.

D2 (US-A-6 083 932) discloses an extract of ginseng (HT1001) for the treatment of conditions coming under the generic heading of dementia, and also for the treatment of Parkinson's disease, attention-deficit syndrome, strokes and depression. However, according to ICD-10 these conditions are not classified under the psychotic disorder of "schizophrenia" - and, therefore, are not within the scope of the present application.

D3 (WO-A-0 004 912) relates to the use of a ginseng extract for the treatment of dementia, referring in particular to improved learning and memory. However, schizophrenia is clearly defined as a different disease from dementia.

D4 (WO-A-9 966 914) discloses a combination of *Hypericum* and L-carnitine for the prophylaxis and treatment of anxiety or depression; in the light of the above remarks, said combination is not within the scope of the present application.

D5 (WO-A-9 940 905) discloses the use of hyperforin and extracts containing hyperforin for the treatment and prophylaxis of dementing diseases. The use thereof in schizophrenia is not disclosed in said document, nor is it obvious therefrom.

/...

D6 (EP-A-599 307) relates to a *Hypericum* extract containing a raised level of hypoforin for use as a psychovegetative and anti-depressant drug. However, the use in schizophrenia as per the claims of the present application does not concern a psychovegetatively conditioned dysfunction or depression.

D7 (WO-A-0 002 455) discloses the specific effect of hypericin on the blocking of T-type calcium channels, which is important in the treatment of depressive conditions but is not included in the management of schizophrenia since schizophrenia is not classed as a disorder of the type treated with T-type Ca antagonists.

D8 (DE-A-3 338 995) relates to the use of bilobalid for the treatment of degenerative cerebral disorders which are accompanied by pathological changes in the myelin layer of the nerve fibres. Schizophrenia, however, is not a degenerative disorder of the brain or the nervous system.

3. In the light of the aforementioned documents, it can be conclusively established that the subject matter of the present application is neither disclosed in nor otherwise obvious from the prior art. The requirements of PCT Article 33(2) and PCT Article 33(3) are accordingly satisfied.